

REMARKS

Upon entry of this amendment, claims 127-132 and 134-137 are pending in the instant application. Claims 127 and 134-135 have been amended, and claim 133 has been cancelled. Support for the claim amendments presented herein is found throughout the specification and in the claims as originally filed, at least at page 8, paragraph [0031] and at page 17, paragraphs [0070]-[0072]. Accordingly, the present amendments are fully supported, and no new matter has been added.

Specification Objection

The specification has been objected to because the trademark “SELEX” is not accompanied by the generic terminology wherever it appears in the specification.

The specification has been amended to insert a generic terminology, an aptamer selection process, for the trademark “SELEX” whenever it appears throughout the specification. Applicants respectfully submit that the objection has been overcome and should be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

Claims 127-130, 136 and 137 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6933114 by Lupold et al (“Lupold”). Claims 131-133 and 135 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Lupold in view of Geiger et al. Nucleic Acids Research, 24: 1029-1036 (1996) (“Geiger”). Claims 133 and 134 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Lupold in view of Firer J. Biochem. Biophys. Methods 49: 433-442 (2001) (“Firer”).

Claim 133 is cancelled. These rejections are therefore moot as they apply to claim 133.

Applicants traverse these rejections on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness. A *prima facie* case of obviousness requires that “either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references.” See MPEP 706.02(j) citing *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). Knowledge of the

disclosure provided by the instant application must be put aside when determining whether the claimed invention would have been obvious. *See* MPEP 2142.

To support the conclusion that the claimed invention is directed to obvious subject matter, the Examiner has cited and combined three references. The Lupold, Geiger, and Firer references do not teach methods for identifying an aptamer regulator, wherein the aptamer regulator recognizes and binds to a target such that, upon binding of the aptamer, the target undergoes a conformational change that increases the affinity of the target to bind to its target partner to form a target–target partner complex. Moreover none of these cited references teach or suggest that the target poorly binds or does not bind to the target partner in the absence of the aptamer regulator. The cited references do not teach any aptamers that can induce a conformational change in the target, let alone an aptamer that induces a conformational change in the target to increase the binding affinity of the target to its partner.

In fact, no combination of these references produces methods for identifying an aptamer regulator that can induce a conformational change in the target to increase the binding affinity of the target to its partner. The Lupold reference merely describes aptamers that bind to Prostate Specific Membrane Antigen (PSMA). Lupold does not teach or suggest a target partner that binds to or otherwise interacts with PSMA, nor does Lupold teach or suggest an aptamer regulator that can induce a conformational change in a target, like PSMA. Therefore, there is no objective reason based on the teachings of Lupold that would lead a skilled artisan to try to identify an aptamer regulator that can induce a conformational change in the target to increase the binding affinity of the target to its partner. A skilled artisan seeking to identify and produce aptamer regulators that induce a conformational change in a target would have no motivation or objective reason to even turn to the teachings of Lupold.

The addition of the Geiger reference fails to remedy the deficiencies in the teachings of Lupold. Geiger merely describes aptamers that bind L-arginine with a high affinity. Geiger is silent regard to the use of an aptamer to increase the binding affinity of the target to its partner by inducing a conformational change in the target, let alone a method for identifying such an aptamer regulator.

Similar to Geiger, the Firer reference also fails to remedy the deficiencies in the teachings of Lupold. Firer is merely a review article that describes the chemical effect of various elution buffers on protein-protein interactions. Firer does not teach or suggest any aptamers, any

methods for identifying any aptamer regulators, nor any methods for identifying an aptamer regulator that can induce a conformational change in the target to increase the binding affinity of the target to its partner.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one ordinary skill in the art. *See* MPEP §2143.01, citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007). Furthermore, a statement that modifications of the prior art to meet the claimed invention would have been “well within the ordinary skill of the art at the time the claimed invention was made” because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *See* MPEP §2143.01, citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993).

There is no objective reason provided by the Lupold, Geiger and Firer references, alone or in combination, that would lead the skilled artisan to combine these references, nor is there any evidence that the resultant combination of these references would have been predictable from the teachings of these references. Moreover, these references fail to provide the skilled artisan with a reasonable expectation that the method recited by the claims presented herein would successfully produce an aptamer regulator that induces a conformational change in the target to increase the binding affinity of the target to its partner.

Thus, any suggestion that the methods recited by the amended claims presented herein would have been obvious is an improper application of hindsight based on Applicants' disclosure in the instant application. As such, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness and request that this rejection be withdrawn.

CONCLUSION

Applicants submit that the claims are not obvious in view of the cited reference. Accordingly, reconsideration of the rejection and allowance of the claims at an early date are earnestly solicited.

If there are any questions regarding this Amendment and Response or if the undersigned can be of assistance in advancing the application to allowance, please contact the undersigned at the number set forth below.

Respectfully submitted,

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Dated: July 18, 2011

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